

Supplemental Material

Mathematical transmission model: It is relatively easy to show that if $\lambda(R, T)$ represents the adult mosquito birth rate, $\mu(T)$ the per capita death rate and we assume a fixed duration of latency in humans, the system dynamics can be described by the coupled delay-differential equations, representing a deterministic disease model in a static environment,

$$S_M' = \lambda(R, T) - a(T)b_1 I_H S_M / N - \mu(T)S_M,$$

$$E_M' = a(T)b_1 I_H S_M / N - \mu(T)E_M - a(T)b_1 I_H (t - \tau_M(T))S_M(t - \tau_M(T))l_M(T) / N,$$

$$I_M' = a(T)b_1 I_H (t - \tau_M(T))S_M(t - \tau_M(T))l_M(T) / N - \mu(T)I_M,$$

$$S_H' = -a(T)b_2 I_M S_H / N,$$

$$I_H' = a(T)b_2 I_M (t - \tau_H)S_H(t - \tau_H) / N - \gamma I_H,$$

where the biting rate, mortality hazard (hence daily survival probability) and duration of the sporogonic cycle depend on temperature T (see Supplemental Material, Table 1) (Martens 1998) and all other parameters are defined in Supplemental Material, Table 2 (with baseline numerical values in Supplemental Material, Table 3). Vector parameters are estimated for *Anopheles maculipennis* (Martens 1998).

We write the birth rate of adult mosquitoes as $\lambda(R, T) = Bp_E(R)p_L(R)p_L(T)p_P(R)/(\tau_E + \tau_L(T) + \tau_P)$ where B is the number of eggs laid per adult per oviposition, p_E , p_L and p_P are the daily survival probabilities of eggs, larvae and pupae and τ_E , τ_L and τ_P are the durations of each of these stages. We assume that B is independent of environmental conditions, development times in each stage are dependent only on temperature if there is sufficient rainfall to sustain development and independent effects of temperature and rainfall on the daily survival probability of larvae. Data from Depinay et al. (2004) for the development times from eggs to larvae and pupae to adults suggest that these are approximately independent of temperature, while the development time from larvae to pupae varies with temperature as $\tau_L(T) = 1/(\alpha T + \beta)$ (Craig et al. 1999; Jepson et al. 1947). Although rainfall has been shown to generally increase malaria

prevalence (Sutherst 2004), it has also been reported that excessive rainfall can reduce transmission, with a suggested cause being the flushing out of aquatic breeding habitats (Jepson et al. 1947; Paaijmans et al. 2007). The simplest non-linear model for the dependence of daily survival probabilities on daily rainfall R (in mm) describing this process is, for the survival of eggs,

$$p_E(R) = \left(4p_{ME} / R_{LE}^2\right)R(R_{LE} - R)$$

where p_{ME} is the peak daily survival probability (corresponding to optimum rainfall for proliferation) and R_{LE} is the rainfall threshold beyond which wash-out effects from excessive rainfall cause no eggs to survive. We assume analogous functional forms for larvae and pupae and identical wash-out limits. Parameterising this model highlights the difficulty in quantifying the effects of rainfall on mosquito development and this remains an area where considerably more data is required. It is important to recognise the role of mathematical modelling in directing such data collection by highlighting areas where improved data quality will lead to better validated models and more reliable predictions.

Parameterising the rainfall model for immature mosquitoes: Here, we assume that the mosquito surface area in contact with the water surface is a factor of three higher in pupae than larvae (suggesting a daily survival probability also a factor of three higher), eggs have the highest daily survival probability (Depinay et al. 2004) and 15% of eggs become adults (Coutinho et al. 2005). Assuming sufficiently high temperatures, the Garnham criteria requires, on average, a monthly rainfall total exceeding 152mm for malaria transmission (Garnham 1948), equating to approximately 5mm/day, and we assume that the daily survival probability drops to zero when rainfall is an order of magnitude greater than this threshold. Substituting $e^{-(\alpha T + \beta)}$ for the daily survival probability of larvae, together with $\tau_L(T) = 1/(\alpha T + \beta)$, gives the total birth rate $\lambda(R, T)$, while we use the expression in Martens (1998) for the daily survival probability (at constant humidity) to obtain the per capita death rate $\mu(T) = 1/(AT^2 + BT + C)$.

Mosquito population model: For this model, writing down the master equation for $p_M(t)$, the probability that there are M mosquitoes at time t , gives

$$\frac{dp_M(t)}{dt} = \lambda(R, T)p_{M-1}(t) + \mu(T)(M+1)p_{M+1}(t) - (\lambda(R, T) + \mu(T)M)p_M(t)$$

for $M(t) = 0, 1, 2, \dots$ and where $p_{-1}(t) = 0$. Defining the probability generating function $G(z, t) = \sum_{i=0}^{\infty} p_i z^i$, we can show that

$$\frac{\partial G(z, t)}{\partial t} = \lambda(R, T)(z-1)G(z, t) - \mu(T)(z-1)\frac{\partial G(z, t)}{\partial z},$$

which holds in a static (constant R and T) or fluctuating ($R = R(t)$ and $T = T(t)$) environment. In the former case, solving this equation by characteristics (subject to M_0 initial mosquitoes) gives

$$G(z, t) = e^{\frac{\lambda(R, T)}{\mu(T)}(z-1)(1-e^{-\mu(T)t})} \left(1 + (z-1)e^{-\mu(T)t}\right)^{M_0}. \quad [S1c]$$

As $t \rightarrow \infty$, $G(z, t) \rightarrow e^{\frac{\lambda(R, T)}{\mu(T)}(z-1)}$ and thus $p_M(t)$ tends to a Poisson distribution with mean $\lambda(R, T)/\mu(T)$, independent of the initial conditions. Substituting $z = 0$ gives the probability that the mosquitoes become extinct at or before time t , whereupon letting $t \rightarrow \infty$ gives the probability of ultimate extinction as $\exp(-\lambda(R, T)/\mu(T))$.

We can also show that the expected time for mosquito extinction to occur. If T_0 represents the random variable for the time to extinction, we have the distribution function of T_0 as

$$P(T_0 \leq t) = p_0(t) = e^{-\left(\frac{\lambda(R, T)}{\mu(T)}\right)(1-e^{-\mu(T)t})} \left(1 - e^{-\mu(T)t}\right)^{M_0}, \quad [S1d]$$

whereupon differentiating to obtain the probability density function and calculating the average time to extinction in the special case when $M_0 = 1$ gives $t_{ext} = \exp(-\lambda(R, T)/\mu(T))$.

Analysis of the invasion dynamics: Consider the transmission model above during the early stages of an outbreak. In this

regime, $S_H(t - \tau_H)/N \approx 1$ and $S_M(t - \tau_M(T))/M \approx 1$, so that the invasion dynamics are described by

$$\dot{I}_H \approx a(T)b_2I_M(t - \tau_H) - \gamma I_H,$$

$$\dot{I}_M \approx a(T)b_1M(R,T)I_H(t - \tau_M(T))l_M(T)/N - \mu(T)I_M.$$

To solve these equations for the rate of spread in humans, we note, with a view to rewriting these equations as a single matrix equation, that I_H and its derivatives (at any time) depend on 1, $I_M(t)$, $I_M(t - \tau_H)$ and $\dot{I}_M(t)$, giving a dependence on four unknowns with two independent equations. Differentiating and considering the resultant equation, as well as that for $I_H(t)$, at time $t + \tau_H$ gives

$$\frac{dI_H(t + \tau_H)}{dt} = a(T)b_2I_M(t) - \gamma I_H(t + \tau_H),$$

$$\frac{dI_M(t)}{dt} = \left(\frac{a(T)b_1M(R,T)}{N} \right) I_H(t - \tau_M)l_M(T) - \mu(T)I_M - a(T)b_2\mu(T)I_M(t) - \gamma \dot{I}_H(t + \tau_H),$$

$$\frac{d^2I_H(t + \tau_H)}{dt^2} = \left(\frac{a(T)^2b_1b_2M(R,T)}{N} \right) I_H(t - \tau_M)l_M(T),$$

so that I_H and its derivatives now depend only on 1, $I_M(t)$ and $\dot{I}_M(t)$ and we have three independent equations, sufficient to find a unique solution for $I_H(t)$. Rewriting as a matrix equation and expanding the resulting determinant allows us to derive an ODE for the number of infectious humans as

$$\ddot{I}_H(t + \tau_H) + (\mu(T) + \gamma)\dot{I}_H(t + \tau_H) + \mu(T)\gamma(I_H(t + \tau_H) - R_0(T)I(t - \tau_M(T))) = 0.$$

Substituting the trial solution $I_H(t) = e^{rt}$ (with growth rate r) gives

$$r^2e^{r\tau_H} + (\mu(T) + \gamma)re^{r\tau_H} + \mu(T)\gamma(e^{r\tau_H} - R_0(T)e^{-r\tau_M(T)}) = 0,$$

which reduces to the standard growth rate equation for the SEIR model when $\tau_H = 0$.

Supplemental Material References

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Supplemental Material, Table 1. Functional forms for quantities in the transmission model

Parameter	Functional form	Units
$a(T)$	$\frac{T - T_1}{D_1}$	Per day
$\mu(T)$	$\frac{1}{AT^2 + BT + C}$	Per day
$\tau_M(T)$	$\frac{DD}{T - T_{min}}$	Days

Supplemental Material, Table 2. Transmission model parameter definitions

Parameter	Definition (and units)
$\lambda(R, T)$	Adult mosquito birth rate per day
$\mu(T)$	Adult mosquito per capita death rate (per day)
$a(T)$	Mosquito biting rate per day
b_1	Proportion of bites by susceptible mosquitoes on infected humans that produce infection
$\tau_M(T)$	Duration of the sporogonic cycle (days)
$l_M(T)$	Survival probability of infected mosquitoes over the incubation period of the parasite
b_2	Proportion of bites by infectious mosquitoes on susceptible humans that produce infection
τ_H	Latent period of infection within humans (days)
$1/\gamma$	Human average duration of infectiousness (days)
$M(t)$	Total number of mosquitoes ($S_M(t) + E_M(t) + I_M(t)$)
N	Total number of humans ($S_H(t) + I_H(t) + R_H(t)$)

Supplemental Material, Table 3. Baseline parameter values of the transmission model

Parameter	Assumed value	Units
B_E	200	Dimensionless
p_{ME}	0.9	Dimensionless
p_{ML}	0.25	Dimensionless
p_{MP}	0.75	Dimensionless
R_L	50	mm
τ_E	1	days
α	0.00554	(°C days) ⁻¹
β	-0.06737	(days) ⁻¹
τ_P	1	Days
T_1	19.9	°C
D_1	36.5	°C days
b_1	0.04	Dimensionless
A	-0.03	(°C ² days) ⁻¹
B	1.31	(°C days) ⁻¹
C	-4.4	days ⁻¹
b_2	0.09	Dimensionless
τ_H	10	days
DD	111 (<i>P. falciparum</i>) 105 (<i>P. vivax</i>)	°C days
T_{\min}	16 (<i>P. falciparum</i>) 14.5 (<i>P. vivax</i>)	°C
γ	1/120	days ⁻¹

Supplemental Material, Figure 1: $R_0(T)$ as a function of increasing variability in rainfall ε (from [3]) for $P.$

falciparum in Tanzania

